IN THE CLAIMS:

Please cancel claims 1-31.

Please add the following new claims:

32. A diagnostic method for indirectly determining the presence of lipidic particles in cell membranes from a sample suspected of having anti-lipidic particle antibodies from an individual suspected of suffering primary antiphospholipid syndrome or a disease associated with secondary antiphospholipid syndrome, wherein the presence of said lipidic particles in cell membranes allows diagnosis of whether said individual is developing an illness associated with the presence of antiphospholipid antibodies though said individual does not present anti-cardiolipin antibodies, lupus anti-coagulant, anti-DNA or anti-nuclear antibodies, comprising:

a) contacting an antigen having lipidic particles with the sample suspected of having anti-lipidic particle antibodies from said individual, under conditions effective to permit binding of anti-lipidic particle antibodies present in the sample to the antigen having lipidic particles thereby forming a first mixture;

b) adding to the first mixture a detectable-labeled reagent useful for detecting binding of anti-lipidic particle antibodies to the antigen having lipidic particles thereby forming a second mixture;

c) detecting the presence of anti-lipidic particle antibodies in the sample bound to the antigen having lipidic particles in the second mixture, wherein said detection of anti-lipidic particle antibodies bound to the antigens having lipidic particles is an indirect indication of the presence of lipidic particles in cell membranes of said individual; and

d) correlating the presence of anti-lipidic particle antibodies in the second mixture with immune damage in cell membranes having lipidic particles of said individual as one of the first events in illness associated with the presence of antiphospholipid antibodies.

33. The method of claim 32, wherein the antigen having lipidic particles is selected from the group consisting of liposomes, erythrocytes, leukocytes, plaquettes and neoplastic cells, and said antigen is present in one condition selected from the group consisting of antigen bound to solid supports and antigen suspended in an appropriate medium.

34. The method of claim 32, wherein the sample suspected of having anti-lipidic particle antibodies is selected from the group consisting of serum and plasma of said individual.

35. The method of claim 32, wherein the detectable-labeled reagent comprises detectable-labeled polyvalent anti-human immunoglobulins second antibodies which bind to the anti-lipidic particle antibodies.

36. The method of claim 35, wherein the detectable-labeled anti-human immunoglobulins second antibodies comprises at least one anti-human immunoglobulin antibody directed against at least one human immunoglobulin class, and the presence of anti-lipidic particle antibodies is determined as one antibody selected from the group consisting of anti-lipidic particles IgG, IgM and IgA antibodies.

37. The method of claim 32, wherein the detectable-labeled reagent comprises one component selected from the group consisting of enzymes and fluorochromes, said component being attached to one element selected from the group consisting of polyvalent anti-immunoglobulins, anti-IgG, IgM and IgA immunoglobulins second antibodies.

38. The method of claim 32, wherein the detection of the presence of anti-lipidic particle antibodies in the sample from said individual is carried out using a protocol selected from the group consisting of ELISA, cytofluorometry and immunofluorescence.

39. A diagnostic method for directly determining the presence of lipidic particles in cell membranes in a sample of cells suspected of having lipidic particles from an individual suspected of suffering primary antiphospholipid syndrome or a disease associated with secondary antiphospholipid syndrome, wherein the presence of said lipidic particles in cell membranes allows diagnosis of whether said individual is developing an illness associated with the presence of antiphospholipid antibodies though said individual does not present anti-cardiolipin antibodies, lupus anti-coagulant, anti-DNA or anti-nuclear antibodies, comprising:

a) contacting said sample of cells suspected of having lipidic particles with at least a polyclonal or monoclonal antibody having anti-lipidic particle antibodies, under conditions effective to permit binding of lipidic particles contained in the cell sample to anti-lipidic particle antibodies present in polyclonal or monoclonal antibodies thereby forming a first mixture;

b) adding to the first mixture a detectable-labeled reagent useful for detecting the binding of the anti-lipidic particle antibodies to the lipidic particles thereby forming a second mixture;

c) detecting the presence of lipidic particles in the cell sample bound to polyclonal or monoclonal anti-lipidic particle antibodies in the second mixture, wherein said detection of lipidic particles bound to anti-lipidic particle antibodies is a direct indication of the presence of lipidic particles in cell membranes of said individual; and

d) correlating the presence of lipidic particles in the cells of the second mixture with immune damage in cell membranes of said individual due to anti-lipidic particle antibodies produced in said individual as one of the first events in illness associated with the presence of antiphospholipid antibodies.

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40. The method of claim 39, wherein the sample of cells is selected from the group consisting of: microsections of organ tissues, erythrocytes, leukocytes, and plaquettes of said individual and neoplastic cells, and said cells are present in one condition selected from the group consisting of cells bound to solid supports and cells suspended in an appropriate medium.

41. The method of claim 39, wherein the anti-lipidic particle polyclonal antibodies are selected from the group consisting of patient serum and immune animal serum in which anti-lipid particle antibodies have been previously detected, and the monoclonal antibody is an anti-lipidic particle monoclonal antibody obtained from hybridomas producing anti-lipidic particle antibodies.

42. The method of claim 39, wherein the detectable-labeled reagent comprises second antibodies selected from the group consisting of detectable-labeled polyvalent anti-human

immunoglobulin antibodies, animal anti-immunoglobulin antibodies, anti-IgM antibodies and anti-IgG antibodies, depending on the class of the monoclonal antibody which binds to the anti-lipidic particle antibodies.

43. The method of claim 42, wherein the detectable-labeled anti-immunoglobulin second antibodies comprise at least one anti-immunoglobulin antibody directed against at least one immunoglobulin class selected from the group consisting of human immunoglobulin class and immune animal immunoglobulin class, and the presence of anti-lipidic particle antibodies is determined as an antibody selected from the group consisting of anti-lipidic particle IgG, IgM and IgA antibodies.

44. The method of claim 39, wherein the detectable-labeled reagent comprises one component selected from the group consisting of enzymes and fluorochromes, said component being attached to one element selected from the group consisting of polyvalent anti-immunoglobulins, anti-IgG, IgM and IgA immunoglobulin second antibodies.

45. The method of claim 39, wherein the detection of the presence of lipidic particles contained in the sample of cells in the second mixture is carried out using a protocol selected from the group consisting of ELISA, cytofluorometry and immunofluorescence.

46. A kit for use in an assay to indirectly determine the presence of lipidic particles in cell membranes from a sample suspected of having anti-lipidic particle antibodies from an individual suspected of suffering primary antiphospholipid syndrome or one disease associated with secondary antiphospholipid syndrome, wherein the presence of said lipidic particles in cell membranes allows diagnosis of whether said individual is developing an illness associated with the presence of antiphospholipid antibodies though said individual does not present anti-cardiolipin antibodies, lupus anti-coagulant, anti-DNA or anti-nuclear antibodies; comprising:

a) an indicator reagent comprising an antigen having lipidic particles to be contacted with the sample from said individual under conditions effective to permit binding of anti-lipidic particle antibodies present in the sample to the lipidic particles of the antigen;
b) a buffer solution as a medium to allow effective conditions for the binding of the anti-lipidic particle antibodies present in the sample to the lipidic particles of the antigen; and
c) a detectable-labeled reagent useful for detecting the binding of anti-lipidic particle antibodies present in the sample to the lipidic particles of the antigen.

47. The kit of claim 46, wherein the antigen having lipidic particles is selected from the group consisting of liposomes, neoplastic cells, human erythrocytes, human leukocytes, and human plaquettes.

48. The kit of claim 47, wherein said liposomes have lipidic particles induced with one agent selected from the group consisting of divalent cations and drugs producing lupus in humans, and wherein said liposomes are in one condition selected from the group consisting of liposomes bound to microtiter plates with a high lipidic binding property and liposomes suspended in an appropriate medium.

49. The kit of claim 47, wherein said neoplastic cells are bound to one support selected from the group consisting of micro cover glasses and microtiter plates.

50. The kit of claim 47, wherein said erythrocytes, leukocytes, and plaquettes are suspended in an appropriate medium.

51. The kit of claim 48, wherein the appropriate medium is the buffer solution that allows effective conditions for the binding of the anti-lipidic particle antibodies present in the sample to the lipidic particles of the antigen.

52. The kit of claim 46, wherein the buffer solution has a pH in the range of 7.0 to 7.4.

53. The kit of claim 46, wherein the sample is selected from the group consisting of serum and plasma of said individual.

54. The kit of claim 46, wherein the detectable-labeled reagent comprises detectable-labeled polyvalent anti-human immunoglobulin second antibodies which bind to the anti-lipidic particle antibodies.

55. The kit of claim 54, wherein the detectable-labeled anti-human immunoglobulin second antibodies comprise at least one anti-human immunoglobulin antibody directed against at least one human immunoglobulin class and the presence of anti-lipidic particle antibodies is determined as an antibody selected from the group consisting of anti-lipidic particles IgG, IgM and IgA antibodies.

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56. The kit of claim 46, wherein the detectable-labeled reagent comprises one component selected from the group consisting of enzymes and fluorochromes, said component being attached to one element selected from the group consisting of polyvalent anti-immunoglobulins, anti-IgG, IgM and IgA immunoglobulin second antibodies, and where the enzyme is selected from the group consisting of alkaline phosphatase and peroxidase, and the fluorochrome is selected from the group consisting of fluorescein isothiocyanate, phycoerythrin, Cy3 and Percp.

57. The kit of claim 46, further including a blocking solution to prevent false positive results from occurring when microtiter plates are used as a solid support, and at least a sample of a reference serum from a healthy individual as a negative control of the reaction with the antigen containing lipidic particles.

58. The kit of claim 46, further including at least an anti-lipidic particle polyclonal or monoclonal antibody to be reacted with the antigen having lipidic particles in order to confirm whether the anti-lipidic particle antibodies are present or not in said sample.

59. The kit of claim 46, wherein the detection of the presence of anti-lipidic particle antibodies in the sample from said individual is carried out using the protocol selected from the group consisting of liposomal-ELISA, cell-ELISA, immunofluorescence, liposomal-cytofluorometry and cell-cytofluorometry.

60. A kit for use in an assay to directly determine the presence of lipidic particles in a sample of cells from an individual suspected of suffering primary antiphospholipid syndrome or one disease associated with secondary antiphospholipid syndrome, wherein the presence of said lipidic particles in cell membranes allows diagnosis of whether said individual is developing an illness associated with the presence of antiphospholipid antibodies though said individual does not present anti-cardiolipin antibodies, lupus anti-coagulant, anti-DNA or anti-nuclear antibodies, comprising:

a) an indicator reagent comprising at least a polyclonal or monoclonal antibody having anti-lipidic particle antibodies to be contacted with the sample of cells from said individual;

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b) a buffer solution as a medium to allow effective conditions for the binding of the anti-lipidic particle antibodies of the polyclonal or monoclonal antibody to the lipidic particles of the cell sample; and

c) a detectable-labeled reagent useful for detecting the binding of anti-lipidic particle antibodies to the lipidic particles of the cell sample.

61. The kit of claim 60, wherein the sample of cells is selected from the group consisting of microsections of organ tissues from said individual, neoplastic cells and isolated erythrocytes, isolated leukocytes, and plaquettes from said individual.

62. The kit of claim 61, wherein said microsections of organ tissues and the neoplastic cells are bound to one support selected from the group consisting of micro cover glasses and microtiter plates.

63. The kit of claim 61, wherein isolated erythrocytes, isolated leukocytes, or plaquettes are suspended in an appropriate medium.

64. The kit of claim 63, wherein the appropriate medium is the buffer solution that allows effective conditions for the binding of the anti-lipidic particle polyclonal or monoclonal antibodies to the lipidic particles of the cell sample.

65. The kit of claim 60, wherein the buffer solution has a pH in the range of 7.0 to 7.4.

66. The kit of claim 60, wherein the anti-lipidic particle polyclonal antibodies are selected from the group consisting of patient serum and immune animal serum in which anti-lipid particle antibodies have been previously detected, and the monoclonal antibody is an anti-lipidic particle monoclonal antibody obtained from hybridomas producing anti-lipidic particle antibodies.

67. The kit of claim 60, wherein the detectable-labeled reagent comprises second antibodies selected from the group consisting of detectable-labeled polyvalent anti-human immunoglobulin antibodies, animal anti-immunoglobulin antibodies, anti-IgM antibodies and anti-IgG antibodies, depending on the class of the monoclonal antibody which bind to the anti-lipidic particle antibodies.

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68. The kit of claim 67, wherein the detectable-labeled anti-immunoglobulin second antibodies comprise at least one anti-immunoglobulin antibody directed against at least one immunoglobulin class selected from the group consisting of human immunoglobulin class and immune animal immunoglobulin class, and the presence of anti-lipidic particle antibodies is determined as an antibody selected from the group consisting of anti-lipidic particles IgG, IgM and IgA antibodies.

69. The kit of claim 60, wherein the detectable-labeled reagent comprises one component selected from the group consisting of enzymes and fluorochromes, said component being attached to one element selected from the group consisting of polyvalent anti-immunoglobulins, anti-IgG, IgM and IgA immunoglobulin second antibodies, and where the enzyme is selected from the group consisting of alkaline phosphatase and peroxidase,

and the fluorochrome is selected from the group consisting of fluorescein isothiocyanate, phycoerythrin, Cy3 and Percp.

70. The kit of claim 60, further including a blocking solution to prevent false positive results from occurring when microtiter plates are used as a solid support, and at least a sample of a reference serum from a healthy individual as a negative control of the reaction with the lipidic particles of the cell sample.

71. The kit of claim 60, wherein the detection of the presence of lipidic particles contained in the sample of cells from said individual is carried out using a protocol selected from the group consisting of cell-ELISA, immunofluorescence and cell-cytofluorometry.

72. A method for determining the presence of lipidic particles in a human or animal sample of cells, wherein the presence of said lipidic particles in cells is indicative of their physiological status, comprising:

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a) contacting the sample of cells with at least a polyclonal or monoclonal antibody having anti-lipidic particle antibodies, under conditions effective to permit binding of lipidic particles contained in the cell sample to anti-lipidic particle antibodies present in polyclonal or monoclonal antibodies thereby forming a first mixture;

b) adding to the first mixture a detectable-labeled reagent useful for detecting the binding of the anti-lipidic particle antibodies to the lipidic particles thereby forming a second mixture;

c) detecting the presence of lipidic particles in the cell sample bound to polyclonal or monoclonal anti-lipidic particle antibodies in the second mixture, wherein said detection of lipidic particles bound to anti-lipidic particle antibodies is a direct indication of the presence of lipidic particles in cell membranes of said cells; and

d) correlating the presence of lipidic particles in the cell membranes of the cells of the second mixture with the physiological status of said cells.

73. The method of claim 72, wherein the sample of cells is selected from the group consisting of human and animal: microsections of organ tissues, neoplastic cells, erythrocytes,

leukocytes, and plaquettes, and said cells are present in one condition selected from the group consisting of cells bound to solid supports and cells suspended in an appropriate medium.

74. The method of claim 72, wherein the anti-lipidic particle polyclonal antibodies are selected from the group consisting of patient serum and immune animal serum in which anti-lipid particle antibodies have been previously detected, and the monoclonal antibody is an anti-lipidic particle monoclonal antibody obtained from hybridomas producing anti-lipidic particle antibodies.

75. The method of claim 72, wherein the detectable-labeled reagent comprises second antibodies selected from the group consisting of detectable-labeled polyvalent anti-human immunoglobulin antibodies, animal anti-immunoglobulin antibodies, anti-IgM antibodies and anti-IgG antibodies, depending on the class of the monoclonal antibody which bind to the anti-lipidic particle antibodies.

B73 cont'd

76. The method of claim 75, wherein the detectable-labeled anti-immunoglobulin second antibodies comprise at least one anti-immunoglobulin antibody directed against at least one immunoglobulin class selected from the group consisting of human immunoglobulin class and immune animal immunoglobulin class, and the presence of anti-lipidic particle antibodies is determined as an antibody selected from the group consisting of anti-lipidic particle IgG, IgM and IgA antibodies.

77. The method of claim 72, wherein the detectable-labeled reagent comprises one component selected from the group consisting of enzymes and fluorochromes, said component being attached to one element selected from the group consisting of polyvalent anti-immunoglobulins, anti-IgG, IgM and IgA immunoglobulin second antibodies.

78. The method of claim 72, wherein the detection of the presence of lipidic particles contained in the sample of cells in the second mixture is carried out using a protocol selected from the group consisting of cytofluorometry, immunofluorescence and ELISA.

79. A kit for use in an assay to determine the presence of lipidic particles in a human or animal sample of cells, wherein the presence of said lipidic particles in cell membranes is indicative of their physiological status, comprising:
a) an indicator reagent comprising at least a polyclonal or monoclonal antibody having anti-lipidic particle antibodies to be contacted with the sample of cells;
b) a buffer solution as a medium to allow effective conditions for the binding of the anti-lipidic particle antibodies of the polyclonal or monoclonal antibody to the lipidic particles of the cell sample; and
c) a detectable-labeled reagent useful for detecting the binding of anti-lipidic particle antibodies to the lipidic particles of the cell sample.

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80. The kit of claim 79, wherein the sample of cells is selected from the group consisting of human and animal: microsections of organ tissues, neoplastic cells, isolated erythrocytes, isolated leukocytes and including plaquettes.

81. The kit of claim 80, wherein the microsections of human or animal organ tissues and the neoplastic cells are bound to one support selected from the group consisting of micro cover glasses and microtiter plates.

82. The kit of claim 80, wherein human or animal isolated erythrocytes, leukocytes, or plaquettes are suspended in an appropriate medium.

83. The kit of claim 82, wherein the appropriate medium is the buffer solution that allows effective conditions for the binding of the anti-lipidic particle polyclonal or monoclonal antibodies to the lipidic particles of the cell sample.

84. The kit of claim 79, wherein the buffer solution has a pH in the range of 7.0 to 7.4.

85. The kit of claim 79, wherein the anti-lipidic particle polyclonal antibodies are selected from the group consisting of patient serum and immune animal serum in which anti-lipid particle antibodies have been previously detected, and the monoclonal antibody is an anti-lipidic particle monoclonal antibody obtained from hybridomas producing anti-lipidic particle antibodies.

86. The kit of claim 79, wherein the detectable-labeled reagent comprises second antibodies selected from the group consisting of detectable-labeled polyvalent anti-human immunoglobulin antibodies, animal anti-immunoglobulin antibodies, anti-IgM antibodies and anti-IgG antibodies, depending on the class of the monoclonal antibody which bind to the anti-lipidic particle antibodies.

87. The kit of claim 86, wherein the detectable-labeled anti-immunoglobulin second antibodies comprise at least one anti-immunoglobulin antibody directed against at least one immunoglobulin class selected from the group consisting of human immunoglobulin class and immune animal immunoglobulin class, and the presence of anti-lipidic particle antibodies is determined as an antibody selected from the group consisting of anti-lipidic particle IgG, IgM and IgA antibodies.

B73 cont'd

88. The kit of claim 79, wherein the detectable-labeled reagent comprises one component selected from the group consisting of enzymes and fluorochromes, said component being attached to one element selected from the group consisting of polyvalent anti-immunoglobulins, anti-IgG, IgM and IgA immunoglobulin second antibodies, and where the enzyme is selected from the group consisting of alkaline phosphatase and peroxidase, and the fluorochrome is selected from the group consisting of fluorescein isothiocyanate, phycoerythrin, Cy3 and Percp.

89. The kit of claim 79, further including a blocking solution to prevent false positive results from occurring when microtiter plates are used as a solid support, and at least a sample of a reference serum from a healthy individual as a negative control of the reaction with the lipidic particles of the cell sample.

B73 cont'd

90. The kit of claim 79, wherein the detection of the presence of lipidic particles contained in the sample of cells in the second mixture is carried out using a protocol selected from the group consisting of cell-ELISA, immunofluorescence and cell-cytofluorometry.